

What is claimed is:

1. A method of identifying one or more markers for rheumatoid arthritis, wherein each of said one or more markers corresponds to a gene transcript, comprising the steps of:

a) determining the level of one or more gene transcripts expressed in blood obtained from one or more individuals having rheumatoid arthritis, wherein each of said one or more transcripts is expressed by a gene that is a candidate marker for rheumatoid arthritis; and

b) comparing the level of each of said one or more gene transcripts from said step a) with the level of each of said one or more genes transcripts in blood obtained from one or more individuals not having rheumatoid arthritis,

wherein those compared transcripts which display differing levels in the comparison of step b) are identified as being markers for rheumatoid arthritis.

2. A method of identifying one or more markers for rheumatoid arthritis, wherein each of said one or more markers corresponds to a gene transcript, comprising the steps of:

a) determining the level of one or more gene transcripts expressed in blood obtained from one or more individuals having rheumatoid arthritis, wherein each of said one or more transcripts is expressed by a gene that is a candidate marker for rheumatoid arthritis; and

b) comparing the level of each of said one or more gene transcripts from said step a) with the level of each of said one or more genes transcripts in blood obtained from one or more individuals having rheumatoid arthritis,

wherein those compared transcripts which display the same levels in the comparison of step b) are identified as being markers for rheumatoid arthritis.

3. A method of identifying one or more markers of a stage of rheumatoid arthritis progression or regression, wherein each of said one or more markers corresponds to a gene transcript, comprising the steps of:

a) determining the level of one or more gene transcripts expressed in blood obtained from one or more individuals having a stage of rheumatoid arthritis, wherein said one or more individuals are at the same progressive or regressive stage of rheumatoid arthritis, and wherein each of said one or more transcripts is expressed by a gene that is a candidate marker for determining the stage of progression or regression of rheumatoid arthritis, and;

b) comparing the level of each of said one or more gene transcripts from said step a) with

the level of each of said one or more genes transcripts in blood obtained from one or more individuals who are at a progressive or regressive stage of rheumatoid arthritis distinct from that of said one or more individuals of step a),

wherein those compared transcripts which display differing levels in the comparison of step b) are identified as being markers for the stage of progression or regression of rheumatoid arthritis.

4. A method of identifying one or more markers of a stage of rheumatoid arthritis progression or regression, wherein each of said one or more markers corresponds to a gene transcript, comprising the steps of:

a) determining the level of one or more gene transcripts expressed in blood obtained from one or more individuals having a stage of rheumatoid arthritis, wherein said one or more individuals are at the same progressive or regressive stage of rheumatoid arthritis, and wherein each of said one or more transcripts is expressed by a gene that is a candidate marker for determining the stage of progression or regression of rheumatoid arthritis, and;

b) comparing the level of each of said one or more gene transcripts from said step a) with the level of each of said one or more genes transcripts in blood obtained from one or more individuals who are at a progressive or regressive stage of rheumatoid arthritis identical to that of said one or more individuals of step a),

wherein those compared transcripts which display the same levels in the comparison of step b) are identified as being markers for the stage of progression or regression of rheumatoid arthritis.

5. The method of any one of claims 1 - 4, wherein each of said one or more markers identifies one or more transcripts of one or more non immune response genes.

6. The method of any one of claims 1 - 4, wherein each of said one or more markers identifies a transcript of a gene expressed by non-blood tissue.

7. The method of any one of claims 1 - 4, wherein each of said one or more markers identifies a transcript of a gene expressed by non-lymphoid tissue.

8. The method of any one of claims 1 - 4, wherein each of said one or more markers identifies a transcript of a gene selected from the group of genes listed in Table 3M.

9. A method of diagnosing or prognosing rheumatoid arthritis in an individual, comprising the steps of:

5 a) determining the level of one or more gene transcripts in blood obtained from said individual, wherein said one or more gene transcripts correspond to said one or more markers of claim 1 and claim 2, and

b) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from
10 one or more individuals not having rheumatoid arthritis,

wherein detecting a difference in the levels of each of said one or more gene transcripts in the comparison of step b) is indicative of rheumatoid arthritis in the individual of step a).

10. A method of diagnosing or prognosing rheumatoid arthritis in an individual, comprising the steps of:

15 a) determining the level of one or more gene transcripts in blood obtained from said individual, wherein said one or more gene transcripts correspond to said one or more markers of claim 1 and claim 2, and

b) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from
20 one or more individuals having rheumatoid arthritis,

wherein detecting the same levels of each of said one or more gene transcripts in the comparison of step b) is indicative of rheumatoid arthritis in the individual of step a).

11. A method of determining a stage of disease progression or regression in an individual having rheumatoid arthritis, comprising the steps of:

25 a) determining the level of one or more gene transcripts in blood obtained from said individual having rheumatoid arthritis, wherein said one or more gene transcripts correspond to said one or more markers of claim 3 and claim 4, and

b) comparing the level of each if said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood

obtained from one or more individuals who each have been diagnosed as being at the same progressive or regressive stage of rheumatoid arthritis,

wherein the comparison from step b) allows the determination of the stage of rheumatoid arthritis progression or regression in an individual.

5 12. A method of diagnosing or prognosing rheumatoid arthritis in an individual, comprising the steps of:

a) determining the level of one or more gene transcripts expressed in blood obtained from said individual, wherein said one or more gene transcripts correspond to said one or more markers of claim 1 and claim 2, and

10 b) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from one or more individuals having rheumatoid arthritis,

c) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from 15 one or more individuals not having rheumatoid arthritis

d) determining whether the level of said one or more gene transcripts of step a) classify with the levels of said transcripts in step b) as compared with levels of said transcripts in step c),

20 wherein said determination is indicative of said individual of step a) having rheumatoid arthritis.

13. A method of determining a stage of disease progression or regression in an individual having rheumatoid arthritis, comprising the steps of:

a) determining the level of one or more gene transcripts expressed in blood obtained from said individual having rheumatoid arthritis, wherein said one or more gene transcripts 25 correspond to said one or more markers of claim 3 and claim 4, and

b) comparing the level of each of said one or more gene transcripts in said blood according to step a) with the level of each of said one or more gene transcripts in blood from one or more individuals having said stage of rheumatoid arthritis,

c) comparing the level of each of said one or more gene transcripts in said blood 30 according to step a) with the level of each of said one or more gene transcripts in blood from

one or more individuals not having said stage of rheumatoid arthritis,

d) determining whether the level of said one or more gene transcripts of step a) classify with the levels of said transcripts in step b) as compared with levels of said transcripts in step c),

5 wherein said determination is indicative of said individual of step a) having said stage of rheumatoid arthritis.

14. The method of any of claims 9-13, wherein said one or more gene transcripts are transcribed from one or more genes selected from the group consisting of the genes listed in Table 3M.

10 15. The method of any one of claims 1-4 and 9-13, wherein said one or more gene transcripts are transcribed from one or more genes selected from the group consisting of:

- a) non-immune response genes,
- b) genes expressed by non blood tissue, and
- c) genes expressed by non lymphoid tissue.

15 16. The method of any one of claims 1 - 4 and 9 - 13, wherein said blood comprises a blood sample obtained from said one or more individuals.

17. The method of claim 16, wherein said blood sample consists of whole blood.

18. The method of claim 16, wherein said blood sample consists of a drop of blood.

19. The method of claim 16, wherein said blood sample consists of blood that has been lysed.

20 20. The method of claim 16, further comprising the step of isolating RNA from said blood samples.

21. The method of any one of claims 1 - 4 and 9 - 13, wherein the step of determining the level of each of said one or more gene transcripts comprises quantitative RT-PCR (QRT-PCR), wherein said one or more transcripts are from step a) and/or step b) of claims 1 - 4 and 9 - 13.

22. The method of claim 21, wherein said QRT-PCR comprises primers which hybridize to said one or more transcripts or the complement thereof, wherein said one or more transcripts are from step a) and/or step b) of claims 1 - 4 and 9 - 13.

23. The method of claim 22, wherein said primers are 15-25 nucleotides in length.

5 24. The method of claim 22, wherein said primers hybridize to one or more genes selected from the group of genes listed in Table 3M, or the complement thereof.

25. The method of any one of claims 1 - 4 and 9 - 13, wherein the step of determining the level of each of said one or more gene transcripts comprises hybridizing a first plurality of isolated nucleic acid molecules that correspond to said one or more transcripts, to an array
10 comprising a second plurality of isolated nucleic acid molecules.

26. The method of claim 25, wherein said first plurality of isolated nucleic acid molecules comprises RNA, DNA, cDNA, PCR products or ESTs.

27. The method of claim 25, wherein said array comprises a plurality of isolated nucleic acid molecules comprising RNA, DNA, cDNA, PCR products or ESTs.

15 28. The method of claim 27, wherein said array comprises two or more of the markers of claim 1.

29. The method of claim 27, wherein said array comprises two or more of the markers of claim 2.

30. The method of claim 27, wherein said array comprises two or more of the markers of
20 claim 3.

31. The method of claim 27, wherein said array comprises two or more of the markers of claim 4.

32. The method of claim 27, wherein said array comprises a plurality of nucleic acid molecules that correspond to genes of the human genome.

33. The method of claim 27, wherein said array comprises a plurality of nucleic acid molecules that correspond to two or more genes selected from the group of genes listed in Table 3M.

34. A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 1.

35. A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 2.

36. A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 3.

37. A plurality of isolated nucleic acid molecules that correspond to two or more of the markers of claim 4.

38. The method of claim 26, wherein said ESTs comprise a length of at least 100 nucleotides.

39. An array consisting essentially of the plurality of nucleic acid molecules of claim 34.

40. An array consisting essentially of the plurality of nucleic acid molecules of claim 35.

41. An array consisting essentially of the plurality of nucleic acid molecules of claim 36.

42. An array consisting essentially of the plurality of nucleic acid molecules of claim 37.

43. A kit for diagnosing or prognosing rheumatoid arthritis comprising:

a) two gene-specific priming means designed to produce double stranded DNA complementary to a gene that corresponds to a marker selected from the group consisting of the markers of claim 1, claim 2, claim 3 and claim 4; wherein said first priming means contains a sequence which can hybridize to RNA, cDNA or an EST complementary to said gene to create an extension product and said second priming means capable of hybridizing to said extension product;

b) an enzyme with reverse transcriptase activity,

c) an enzyme with thermostable DNA polymerase activity, and

d) a labeling means;

wherein said primers are used to detect the quantitative expression levels of said gene in a test subject.

44. A kit for monitoring a course of therapeutic treatment of rheumatoid arthritis,

comprising:

a) two gene-specific priming means designed to produce double stranded DNA complementary to a gene that corresponds to a marker selected from the group consisting of the markers of claim 1, claim 2, claim 3 and claim 4; wherein said first priming means contains a sequence which can hybridize to RNA, cDNA or an EST complementary to said gene to create an extension product and said second priming means capable of hybridizing to said extension product;

b) an enzyme with reverse transcriptase activity,

c) an enzyme with thermostable DNA polymerase activity, and

d) a labeling means;

wherein said primers are used to detect the quantitative expression levels of said gene in a test subject.

45. A kit for monitoring progression or regression of rheumatoid arthritis, comprising:

a) two gene-specific priming means designed to produce double stranded DNA complementary to a gene that corresponds to a marker selected from the group consisting of the markers of claim 1, claim 2, claim 3 and claim 4; wherein said first priming means contains a sequence which can hybridize to RNA, cDNA or an EST complementary to said gene to create an extension product and said second priming means capable of hybridizing to said extension product;

b) an enzyme with reverse transcriptase activity,

c) an enzyme with thermostable DNA polymerase activity, and

d) a labeling means;

wherein said primers are used to detect the quantitative expression levels of said gene in a test subject.

46. The kit of any one of claims 43 - 45 wherein said gene-specific priming means are complementary to a gene selected from the group of genes listed in Table 3M;

47. A plurality of nucleic acid molecules that identify or correspond to two or more genes selected from the group of genes listed in Table 3M.

5 48. The method of claim 27, wherein said ESTs comprise a length of at least 100 nucleotides.